REMARKS/ARGUMENTS

Claims 1-17, 27, 29, and 37 are under examination and stand substantively rejected. Claims 18-26, 28, and 30-36 were previously canceled. In this Amendment, claims 1, 6, 15, 17, 27, and 37 are amended. Reconsideration is respectfully requested.

Claim Amendments

Support for the amendment to claims 1, 17, 27, and 37 can be found in the specification at, for example, paragraphs [0128]. Claims 6 and 15 is amended to conform antecedent basis. No new matter is introduced.

Claim Objections

Claim 15 is objected to for allegedly being of improper dependent form. Amended claim 15 does not recite the term "agonist." Withdrawal of this objection is respectfully requested.

Rejection Under 35 U.S.C. §112

Claims 2 and 3 were rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enablement. This rejection is traversed.

The rejection is based on the premise that hypocretin is allegedly known to increase feeding behavior, and therefore hypocretin administration will result in increased body weight.

Applicants note that literature which *seems* to indicate that hypocretin (orexin) induces feeding is actually based on the finding that **direct injection** of hypocretin into or adjacent to **known feeding-inducing regions** of the brain can induce feeding. However, hypocretin has been shown to excite virtually all neurons, and hence it is not possible to draw definitive conclusions regarding hypocretin's role on feeding behavior based on these studies.

Moreover, there is considerable evidence establishing that hypocretin in fact does not increase feeding behavior.

For example, hypocretin depleted humans (i.e. narcoleptics) have been well documented to be significantly more obese than control populations, not anorexic *as would be predicted by a feeding inducing role for hypocretin.* See Schuld A, Hebebrand J, Geller F,

Pollmacher T. Increased body-mass index in patients with narcolepsy. Lancet 2000 Apr. 8;355:1274-5 (Attached at Appendix A).

It is also noted that hypocretin knockout mice are also extremely obese, and not extremely thin *as would be predicted by a feeding inducing role for hypocretin.* See Beuckmann CT, Sinton CM, Williams SC, et al. Expression of a poly-glutamine-ataxin-3 transgene in orexin neurons induces narcolepsy-cataplexy in the rat. J. Neurosci. 2004 May 5;24(18):4469-77 (Attached at Appendix B).

What is more, transgenic hypocretin overexpressing mice are resistant to obesity, and not overweight *as would be predicted by a feeding inducing role for hypocretin.* See Funato H, Tsai AL, Willie JT, et al. Enhanced Orexin Receptor-2 Signaling Prevents Diet-Induced Obesity and Improves Leptin Sensitivity. Cell Metabolism 2009 Jan. 7;9(1):64-76 (Attached at Appendix C).

In sum, the literature regarding hypocretin, when considered on the whole, does not support the conclusion that hypocretin is known to increase feeding behavior. Hence, the premise of the enablement rejection (i.e.. hypocretin is known to increase feeding behavior) is unsupported. Withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. §102

Claims 1, 6-17, 27, and 37 were rejected under 35 U.S.C. §102(a) as allegedly anticipated by Stricker-Krongrad "Orexins/hypocretins in the ob/ob mouse: hypothalamic gene expression, peptide content and metabolic effects" Regulatory Peptides 104:11-20 (2002) ["Stricker"]. This rejection is traversed.

According to MPEP 2131, to anticipate a claim, the cited reference must teach all elements of the claim. Stricker does not meet this test.

Amended Independent Claim 1

Amended independent claim 1 is drawn to a method of increasing gross motor activity in an individual. The method includes administering an effective dosage regime of hypocretin-1 or hypocretin 2 to a peripheral tissue in the individual. As explained in the instant specification at paragraph [0128], peripheral tissue refers to tissue other than central nervous system tissue.

In contrast, Stricker describes intracerebroventricular injection of hypocretin. Hence, Stricker does not teach or suggest administration of hypocretin to a peripheral tissue as presently claimed.

Moreover, Stricker describes administration of hypocretin to stimulate food intake. It is well established that new uses are patentable as methods. This fundamental tenet is codified in 35 U.S.C. §100(b) which states that patentable methods include "***a new use of a known process***." Amended claim 1 is drawn to a method of increasing gross motor activity in an individual that includes administering hypocretin to the individual. In contrast, Stricker describes administration of hypocretin to a mouse, but does not teach or suggest that this process can be used to increase gross motor activity as presently claimed.

Because Stricker does not teach or suggest administration of hypocretin to a peripheral tissue, or administration of hypocretin to increase gross motor activity, Stricker does not anticipate amended claim 1. Each of dependent claims 6-16 are novel over Stricker, by virtue of their dependence from amended base claim 1.

Amended Independent Claims 17 and 27

Amended independent claims 17 and 27 are drawn to methods of increasing locomotion in an individual that include administering hypocretin to a peripheral tissue in the individual. As noted above, Stricker describes intracerebroventricular injection of hypocretin to stimulate food intake. Because Stricker does not teach or suggest administration of hypocretin to a peripheral tissue, or administration of hypocretin to increase locomotion, Stricker does not anticipate amended claims 17 and 27.

Amended Independent Claim 37

Amended independent claim 37 is drawn to a method of treating an individual that includes administering an effective dosage regime of hypocretin-1 or hypocretin 2 to a peripheral tissue in the patient. As noted above, Stricker describes intracerebroventricular injection of hypocretin. Because Stricker does not teach or suggest administration of hypocretin to a peripheral tissue, Stricker does not anticipate amended claim 37.

Withdrawal of this rejection is respectfully requested.

First Rejection Under 35 U.S.C. §103

Claims 1, 4-17, 27, and 37 were rejected under 35 U.S.C. §103(a) as allegedly obvious over Stricker in view of Haynes, Peptides 20:1099-1105 (1999) ["Haynes"]. This rejection is traversed.

It is well established that a *prima facie* case of obviousness requires, among other things, that all claim elements are considered when determining patentability against the cited references. Applicants submit that the combination of Stricker and Haynes does not teach or suggest all elements of the amended claims.

As noted above, amended independent claims 1, 17, 27, and 37 involve administration of hypocretin to a peripheral tissue, which Stricker does not disclose. Haynes describes intracerebroventricular administration, and therefore does not remedy the deficiencies of Stricker. Thus, the combination of Stricker and Haynes does not support a *prima facie* case of obviousness for amended independent claims 1, 17, 27, and 37, or claims 4-16 which depend therefrom. Withdrawal of this rejection is respectfully requested.

Second Rejection Under 35 U.S.C. §103

Claims 1, 6-17, 27, 29, and 37 were rejected under 35 U.S.C. §103(a) as allegedly obvious over Stricker in view of Ida, Brain Res. 821(2):526-529 (1999) ["Ida"]. This rejection is traversed.

As noted above, amended independent claims 1, 17, 27, and 37 involve administration of hypocretin to a peripheral tissue, which Stricker does not disclose. Ida describes cerebroventricular administration, and therefore does not remedy the deficiencies of Stricker. Thus, the combination of Stricker and Ida does not support a *prima facie* case of obviousness for amended independent claims 1, 17, 27, and 37, or claims 6-16 which depend therefrom. Withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,

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Attachments

Appendix A
Appendix B
Appendix C

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